REMARKS/ARGUMENTS

Claims 12, 14, 15 and 17-34 are under examination in the application. The Office Action mailed on May 28, 2009 includes the following rejections:

1. Claims 12, 20 and 21 remain rejected under 35 U.S.C. § 112, first paragraph, written description.

2. Claims 28-34 are rejected under 35 U.S.C. § 112, first paragraph, written description.

3. Claims 12, 14, 17-18, 20, 22-27 are rejected under 35 U.S.C. § 112, first paragraph, enablement.

4. Claims 12, 14, 18-22 and 24-27 are rejected under 35 U.S.C. § 103(a), as being unpatentable.

5. Claims 15, 17 and 23 are rejected under 35 U.S.C. § 103(a), as being unpatentable.

Claim Rejections – Claims 12, 20 and 21 remain rejected under 35 U.S.C. § 112, first paragraph, written description.

Applicants respectfully submit that the claims as amended overcome the rejection, namely, the language "reducing" and "reduces" find support in Figures 10A-10C, which show that there is a reduction in the extensive bilateral striatal lesions. Support for the claim language "reducing" as relates to cell death may also be found in, e.g., paragraph [0164], "GW5074 reduced MPP^+-induced cell death. Similarly, as shown in FIG. 9B, GW5074 also reduced methylmercury-induced cell death." (Emphasis added).

Therefore, amended claims 12, 20 and 21 are supported by the specification and comply fully with 35 U.S.C. § 112, first paragraph. Applicants respectfully request the Examiner withdraw the rejection of claims 12, 20 and 21 under 35 U.S.C. § 112, first paragraph.

Claim Rejections – Claims 28-34 are rejected under 35 U.S.C. § 112, first paragraph, written description.

Applicants respectfully submit that the present application supports claims 28-34 in compliance with 35 U.S.C. § 112, first paragraph.

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-564, 19 USPQ2d 1111, 1116-117 (Fed. Cir. 1991) and In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983).

As noted in the Office Action, page 3, Figures 10A-10C of the specification show that there is a reduction in the extensive bilateral striatal lesions. Therefore, the specification supports the "reducing" or "reduces" language. Support for the claim language "reducing" as relates to cell death may be found in, e.g., paragraph [0164], "GW5074 reduced MPP^+-induced cell death. Similarly, as shown in FIG. 9B, GW5074 also reduced methylmercury-induced cell death." (Emphasis added). Therefore, the specification provides literal support for term "reduce" or "reducing" cell death in the claims.

Therefore, claims 28-34 are supported by the specification and comply fully with 35 U.S.C. § 112, first paragraph. Applicants respectfully request the Examiner withdraw the rejection of claims 28-34 under 35 U.S.C. § 112, first paragraph.

Claim Rejections – Claims 12, 14, 17-18, 20, 22-27 are rejected under 35 U.S.C. § 112, first paragraph, enablement.

Applicants respectfully submit that the present application is enabled to support claims 12, 14, 17-18, 20, 22-27 and fully complies with 35 U.S.C. § 112, first paragraph. Applicants traverse the rejection as the skilled artisan would know which compounds that are derivatives, complexes, solvates or hydrates could be used after reading the present invention. However,

solely to move prosecution forward Applicants have amended the claims; no equivalents are disclaimed by this amendment. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejections – Claims 12, 14, 18-22 and 24-27 are rejected under 35 U.S.C. § 103(a), as being unpatentable.

The Office Action also rejects claims 12, 14, 18-22 and 24-27 as unpatentable under 35 U.S.C. § 103(a) over Sweatt, et al., (Sweatt) in U.S. Patent Publication 2002/0058699 and Hall-Jackson, et al., (Jackson) in Paradoxical activation of Raf by a novel Raf inhibitor, Chemistry & Biology, August 1999, Vol. 6 pp. 559-568. Applicants respectfully submit that the art cited fails to provide a prima facie case of obviousness.

Statement of Joint Inventorship. Applicants were advised in the Office Action of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a). Applicants hereby re-state that the assignment rights for each inventor were commonly owned by the assignee at the time of each invention as claimed pursuant to 37 C.F.R. § 1.56.

In *KSR Int'l. Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 (2007), the Court stated that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." Id. at 1741 (emphasis added).

As the PTO recognizes in MPEP § 2142:

> *... The examiner bears the initial burden of factually supporting any prima facie conclusion of obviousness. If the examiner does not produce a prima facie case, the applicants are under no obligation to submit evidence of nonobviousness...*

Neurodegenerative diseases are a subset of neurological diseases characterized by an abnormal loss of neurons. Epilepsy is a neurological disease but not a neurodegenerative disease because epilepsy does not directly cause neuronal loss. The defining feature of eplilepsy is excessive brain neuronal excitability (not neuronal loss). Sweatt proposed that increased activation of MAPK can reduce the excessive excitation of neurons that occurs in seizure disorder/epilepsy. Since c-Raf inhibitors would reduce MAPK activity, Sweatt, suggests that such compounds may be useful in treating seizure disorders (disorders resulting from excessive neuronal excitability). The present invention is directed to the use of c-Raf inhibitors to treat a different class of neurological disorders, specifically neurodegenerative disorders, of which eplilepsy/seizure is not part. Excessive neuronal excitability is not a feature of neurodegenerative diseases. On the contrary, patients with neurodegenerative diseases generally display sharply reduced brain neuronal activity.

Hall-Jackson teaches that when transformed cells are treated with c-Raf / B-Raf inhibitors such as ZM336372, a paradoxical activation of c-Raf results. The authors conclude that "compounds which inhibit the kinase activity of Raf may not be useful as anticancer drugs" page 566, right hand column. Hall-Jackson teaches that the strong feedback loops of raf may actually cause inhibitors to have the adverse effect of increasing raf activity, that is, it teaches against their use. Furthermore, Hall-Jackson does not address the issue of neurological or neurodegenerative diseases. The present inventors have found nothing paradoxical about their findings, which are, that Raf inhibitors reduces neuronal death and are therefore useful to treat neurodegenerative diseases. Therefore, the skilled artisan would understand from reading Hall-Jackson that raf inhibitors are counter-productive and would not use them, alone or in combination with Sweatt, because they are not useful for their intended purpose.

Accordingly, claims 12, 14, 18-22 and 24-27 are not anticipated by, or rendered obvious from Sweatt and Hall-Jackson or any combination thereof. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 103(a).

Claim Rejections – Claims 15, 17 and 23 are rejected under 35 U.S.C. § 103(a), as being unpatentable

The Office Action also rejects claims 15, 17 and 23 as unpatentable under 35 U.S.C. § 103(a) over Sweatt, et al., (Sweatt) in U.S. Patent Publication 2002/0058699 and Hall-Jackson, et al., (Jackson) in Paradoxical activation of Raf by a novel Raf inhibitor, Chemistry & Biology, August 1999, Vol. 6 pp. 559-568, as applied to claims 12, 14, 18-22 and 24-27 above, and further in view of Varga (involvement of Raf-1 in chronic s-opioid receptor agonist-mediated adenylyl cyclase superactivation, European Journal of Pharmacology 451, 2002, pp. 101-102).

Applicants traverse the rejection and incorporate herein by reference their arguments against Sweatt and Hall-Jackson. Varga is added to provide a teaching that in cultured cells GW5074 reduces the overactivation of adenyl cyclase in response to treatment with synthetic opioid. This finding has no bearing whatsoever on neurodegeneration or the use of GW5074 as a therapeutic drug for treating neurodegenerative diseases. First, the Varga reference does not refer to any neurological or neurodegenerative diseases; as such, the skilled artisan would have not motivation to attempt to use it for the treatment of neurodegeneration. At most, Varga suggests that GW5074 could have value in treating opioid addiction. Therefore, nothing in Sweatt or Hall-Jackson helps overcome this deficiency in Varga.

Accordingly, claims 15, 17 and 23 are not anticipated by, or rendered obvious from Sweatt, Hall-Jackson and Varga or any combination thereof. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In light of the foregoing, Applicants submit that claims 12, 14, 15 and 17-34 are in condition for allowance, and an early Notice of Allowance of all pending claims is respectfully requested.

This paper is being filed with all required fees; however, if any additional fees are necessary the Commissioner is hereby authorized to charge any fees, including those for an extension of time, to Chalker Flores, LLP's Deposit Account No. 50-4863.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: August 28, 2009

Respectfully submitted,

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